# Hematologic Malignancy Detection | LeXHema Panel v2.0

## Background

Hematologic malignancies are a group of clonal malignant diseases originating from the hematopoietic system, characterized by high heterogeneity. They include major types such as leukemia, lymphoma, multiple myeloma, and myelodysplastic syndromes. Different hematologic malignancies exhibit significant variations in their molecular genetic features, involving a range of genetic alterations such as base substitutions, insertions/deletions, copy number variations (CNVs), and gene fusions. Consequently, comprehensive and precise molecular detection is crucial for the accurate diagnosis, targeted treatment strategy formulation, and minimal residual disease (MRD) monitoring of these disorders.

Traditional detection techniques—such as FISH, qPCR, and Sanger sequencing—offer certain advantages for detecting specific mutations. However, they often cover only a limited set of genes or known hotspot mutations, making it challenging to fully decipher the complex spectrum of genetic abnormalities. This is particularly problematic for detecting low-frequency mutations and discovering novel fusion genes. The emergence of high-throughput sequencing (NGS) technology has delivered a breakthrough, enabling panoramic molecular profiling of hematologic malignancies.

DNA-based detection can cover coding regions as well as portions of intronic regions, allowing for comprehensive analysis of point mutations, indels, CNVs, and fusion breakpoints. This approach is well-suited for screening both known and potential pathogenic variants. However, gene fusion detection via DNA methods relies on intronic probes, which can be compromised by the extensive length and repetitive nature of intronic regions, potentially resulting in missed fusion events. In contrast, RNA-based detection directly targets fusion gene detection at the transcript level. It not only precisely identifies genuine fusion events and their partner genes but also evaluates whether these fusions result in aberrant transcripts, thereby elucidating their functional impact. Thus, the integration of both DNA and RNA workflows achieves a multidimensional analysis of genetic alterations: DNA detection provides broad coverage for mutation screening, while RNA detection accurately confirms fusion expression and functionality. Together, they ensure comprehensive detection and enhanced accuracy of results.

## Introduction

**LeXHema Panel v2.0** targets 481 genes associated with hematologic malignancies, comprehensively covering a wide range of genetic alterations including base substitutions, insertions/deletions, amplifications, and gene fusions.

**This panel consists of two components:**

LeXHema Panel v2.0_DNA Tube: Covers 1.7 Mb of genomic regions, including full coding regions of 436 genes, partial intronic regions of 12 genes, and the *IGH* Switch regions.

LeXHema Panel v2.0_RNA Tube: Covers 146 genes, optimized for fusion gene detection.

By integrating multi-omics approaches, employing a highly targeted design, and enhancing clinical utility, **LeXHema Panel v2.0** offers an efficient and cost-effective solution for precision diagnosis, treatment planning, and longitudinal management of hematologic malignancies.

# Feature

## Comprehensive Multi-type Mutation Coverage

- Encompasses 481 hematologic malignancy-related genes, enabling thorough analysis of base substitutions, indels, amplifications, and gene fusions.

## Dual Workflow for Enhanced Accuracy

- RNA workflow compensates for the limitations of the DNA workflow by accurately identifying fusion gene partners and validating the functional impact of fusion events. The synergistic use of both workflows ensures comprehensive and precise detection.

## Flexible Customization

- Supports flexible subdivision into multiple sub-panels or the addition of target genes, allowing adaptation to diverse hematologic malignancy diagnostic needs in both research and clinical applications.

# Performance

## LeXHema Panel v2.0_DNA

### Capture Performance

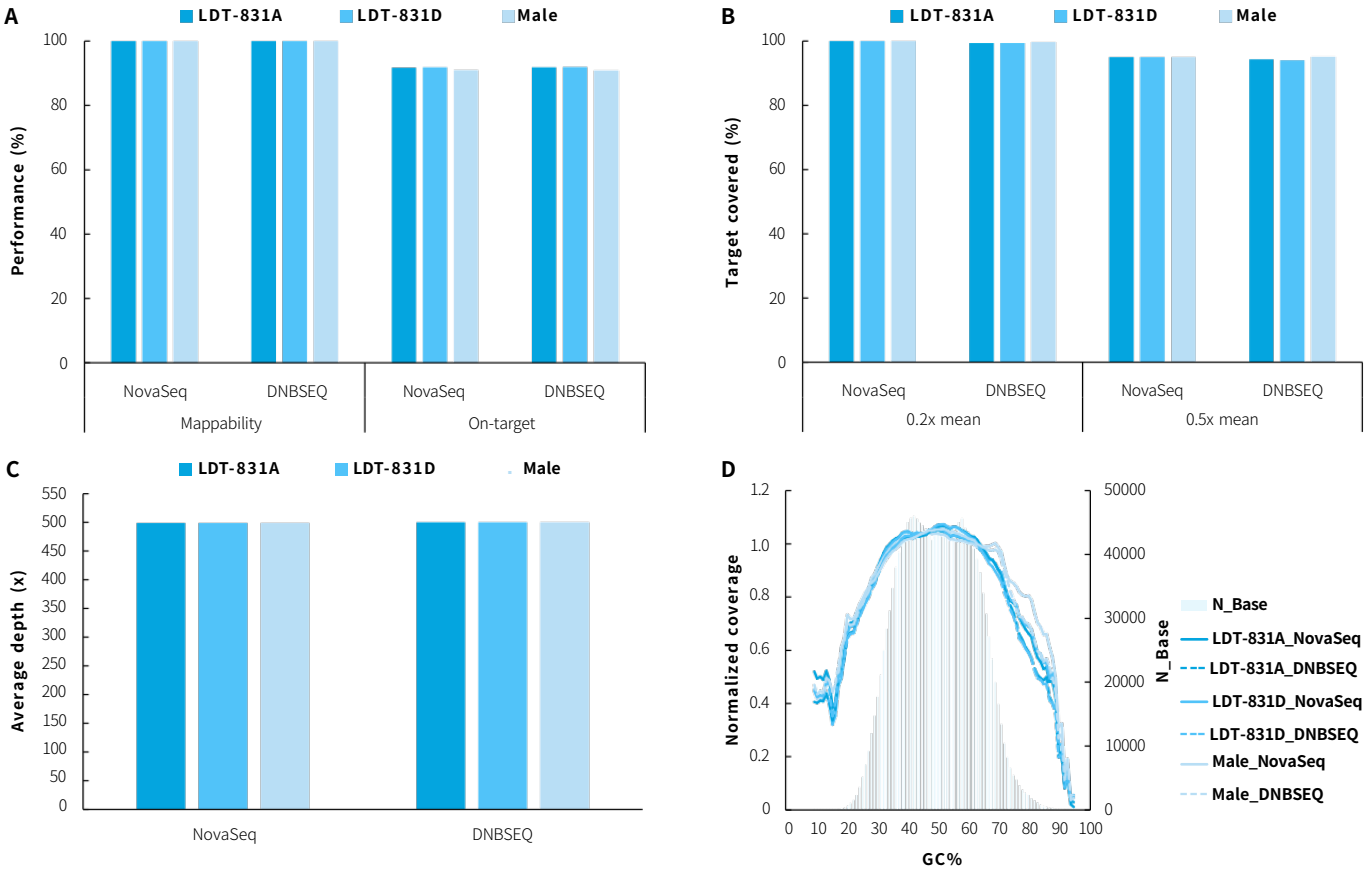


**Figure 1. Capture performance of LeXHema Panel v2.0_DNA applied to various types of gDNA samples. A.** Mappability & On-target rate; **B.** Target covered; **C.** Average sequencing depth after deduplication; **D.** GC bias. Using 50 ng of various gDNA samples, pre-libraries were prepared with the LexPrep EZ DNA Library Preparation Kit coupled with the LexPrep Universal Stubby Adapter (UDI) Module, followed by hybrid capture using LeXHema Panel v2.0_DNA with LexPrep Hybrid Capture Reagents. Sequencing was performed on both NovaSeq 6000 (PE150) and DNBSEQ-T7 (PE150) platforms, with a random subset of 1.3 Gb used for data analysis.

**Note:** LDT-831: hematologic malignancy gDNA quality control (LDT Bioscience; LDT-831A: AF = 5%; LDT-831D: AF = 0%). Male: human genomic DNA standard (Promega, G1471).

## Stable Detection of Multiple Mutation Types

**Table 1. Detection of various mutation types in different standard samples using LeXHema Panel v2.0_DNA.**

| Type | Variant | LDT-831A | | | LDT-831D | | | Male | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Reference | Observed | | Reference | Observed | | Reference | Observed | |
| | | | NovaSeq | DNBSEQ | | NovaSeq | DNBSEQ | | NovaSeq | DNBSEQ |
| SNV | *JAK2* V617F | 5% | 4.4% | 4.9% | 0% | 0% | 0% | 0% | 0% | 0% |
| SNV | *KIT* D816V | 5% | 5.1% | 3.6% | 0% | 0% | 0% | 0% | 0% | 0% |
| SNV | *TP53* R175H | 5% | 3.5% | 6.4% | 0% | 0% | 0% | 0% | 0% | 0% |
| SNV | *RUNX1* R201Q | 5% | 5.7% | 4.0% | 0% | 0% | 0% | 0% | 0% | 0% |
| SNV | *IDH1* R132H | 5% | 5.9% | 4.3% | 0% | 0% | 0% | 0% | 0% | 0% |
| Insertion | *FLT3* E598_Y599insFDFREYE | 5% | 3.8% | 3.1% | 0% | 0% | 0% | 0% | 0% | 0% |
| Fusion | *BCR-ABL1* (e14a2) | 5% | 4.4% | 3.4% | 0% | 0% | 0% | 0% | 0% | 0% |
| Fusion | *CCDC6-RET* | 5% | 12.5% | 20.2% | 0% | 0% | 0% | 0% | 0% | 0% |

# LeXHema Panel v2.0_RNA

## Capture Performance

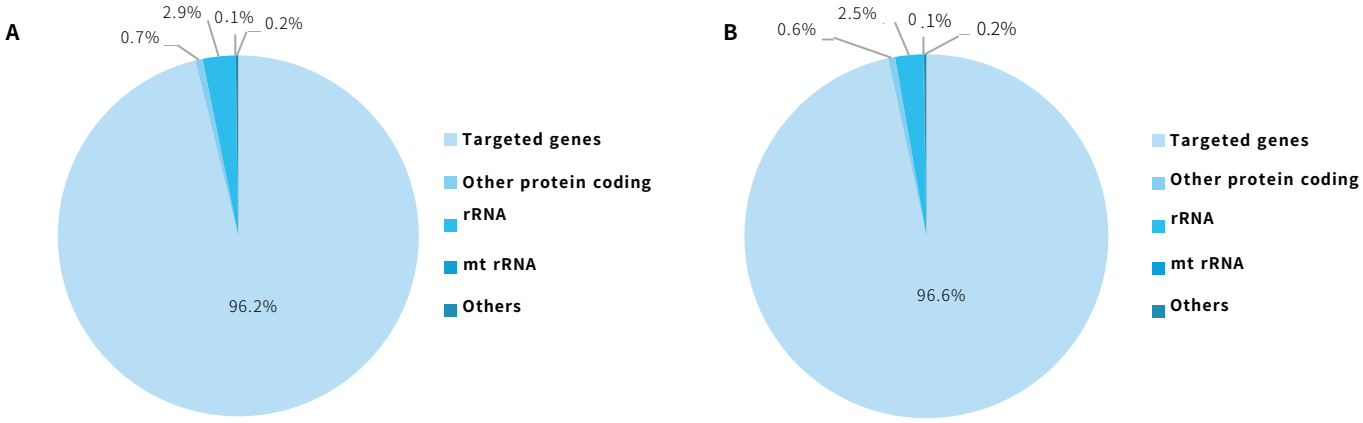


**Figure 2. Composition of capture sequencing data using LeXHema Panel v2.0_RNA.** For the K562 cell line RNA (50 ng), pre-libraries were prepared using the LexPrep Total RNA-To-DNA Module coupled with the LexPrep DNA Library Preparation Kit v2, followed by hybrid capture with LeXHema Panel v2.0_RNA and LexPrep Hybrid Capture Reagents. Sequencing was performed on NovaSeq 6000 (PE150) **(A)** and DNBSEQ-T7 (PE150) **(B)**, with analysis performed using Salmon.

**Table 2. Detection of fusion genes in K562 cell line RNA using LeXHema Panel v2.0_RNA.**

| Fusion type | Platform | Split reads1 | Split reads2 | Discordant mates | Coverage1 | Coverage2 |
|---|---|---|---|---|---|---|
| *BCR-ABL1* | NovaSeq | 298 | 214 | 14 | 948 | 882 |
| | DNBSEQ | 223 | 204 | 10 | 852 | 849 |
| *NUP214-XKR3* | NovaSeq | 86 | 28 | 6 | 1114 | 30 |
| | DNBSEQ | 87 | 23 | 6 | 1155 | 27 |

**Note:** Data are reported per M read pairs (approximately 0.3 Gb); analysis was performed using Arriba.

# Gene List

## LeXHema Panel v2.0_DNA_436 genes_Full CDS

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ABL1 | ABL2 | ACTB | AKT1 | AKT2 | AKT3 | ALK | AMER1 | ANKRD26 | AP3B1 | APC | AR | ARAF | ARHGAP26 | ARID1A |
| ARID1B | ARID2 | ARID5B | ASXL1 | ASXL2 | ASXL3 | ATG5 | ATM | ATR | ATRX | ATXN1 | AURKA | AURKB | AXIN1 | AXL |
| B2M | BAALC | BAP1 | BARD1 | BCL10 | BCL11A | BCL11B | BCL2 | BCL6 | BCL7A | BCOR | BCORL1 | BIRC3 | BLM | BLNK |
| BRAF | BRCA1 | BRCA2 | BRD4 | BTG1 | BTG2 | BTK | BTLA | CALR | CARD11 | CBFB | CBL | CBLB | CCND1 | CCND2 |
| CCND3 | CCNE1 | CCR4 | CCR7 | CCT6B | CD22 | CD27 | CD274 | CD28 | CD58 | CD70 | CD79A | CD79B | CD83 | CDC42 |
| CDC73 | CDH1 | CDK12 | CDK4 | CDK6 | CDK8 | CDKN1A | CDKN1B | CDKN1C | CDKN2A | CDKN2B | CDKN2C | CEBPA | CEP57 | CHD2 |
| CHD8 | CHEK1 | CHEK2 | CIITA | CKS1B | CREBBP | CRLF2 | CSF1R | CSF3R | CTCF | CTLA4 | CTNNB1 | CUX1 | CXCR4 | CYLD |
| DAXX | DDR2 | DDX3X | DDX41 | DHX15 | DNM2 | DNMT3A | DOT1L | DTX1 | DUSP2 | DUSP22 | EBF1 | ECT2L | EED | EGFR |
| EP300 | EPCAM | EPHA2 | EPHA3 | EPHA5 | EPHA7 | EPOR | ERBB2 | ERBB3 | ERBB4 | ERCC4 | ERG | ESR1 | ETNK1 | ETS1 |
| ETV1 | ETV4 | ETV6 | EZH2 | FAM46C | FANCA | FANCC | FANCD2 | FANCE | FANCF | FANCG | FANCI | FANCJ | FANCL | FANCM |
| FAS | FAT1 | FAT4 | FBXO11 | FBXW7 | FGFR1 | FGFR2 | FGFR3 | FGFR4 | FH | FLCN | FLT1 | FLT3 | FLT4 | FOXO1 |
| FOXO3 | FOXP1 | FYN | GADD45B | GATA1 | GATA2 | GATA3 | GNA11 | GNA13 | GNAQ | GNAS | GNB1 | GRIN2A | HACE1 | HBA1 |
| HBA2 | HBB | HDAC1 | HDAC4 | HDAC7 | HGF | HIST1H1A | HIST1H1C | HIST1H1D | HIST1H1E | HNF1A | HRAS | ID3 | IDH1 | IDH2 |
| IFNAR2 | IGF1R | IGH | IGK | IGL | IGLL5 | IKBKE | IKZF1 | IKZF2 | IKZF3 | IL3 | IL7R | INPP4B | INPP5D | IRF1 |
| IRF4 | IRF8 | ITK | ITPKB | JAK1 | JAK2 | JAK3 | JARID2 | JUN | KAT6A | KDM2B | KDM5A | KDM5C | KDM6A | KDR |
| KIT | KLF2 | KLHL5 | KLHL6 | KMT2A | KMT2B | KMT2C | KMT2D | KRAS | LEF1 | LMO2 | LRP1B | LTB | LYN | LYST |
| MAF | MAFB | MALT1 | MAP2K1 | MAP2K2 | MAP2K4 | MAP3K1 | MAP3K14 | MAPK1 | MCL1 | MDM2 | MDM4 | MED12 | MEF2B | MEF2D |
| MEN1 | MET | MFHAS1 | MGA | MITF | MLH1 | MPL | MSH2 | MSH3 | MSH6 | MTOR | MUTYH | MYB | MYC | MYCL |
| MYCN | MYD88 | NBN | NCKAP1L | NCSTN | NF1 | NF2 | NFE2L2 | NFKB1 | NFKB2 | NFKBIA | NFKBIE | NKX2-1 | NLRC4 | NOTCH1 |
| NOTCH2 | NPM1 | NRAS | NSD1 | NT5C2 | NTRK1 | NTRK3 | NUP98 | P2RY8 | PAG1 | PAK3 | PALB2 | PAX5 | PBRM1 | PC |
| PDCD1 | PDCD1LG2 | PDGFRA | PDGFRB | PDK1 | PHF6 | PIK3CA | PIK3CD | PIK3R1 | PIK3R2 | PIM1 | PLCG1 | PLCG2 | PML | PMS2 |
| POLE | POT1 | POU2AF1 | PPM1D | PPP2R1A | PRDM1 | PRF1 | PRKCB | PRPF8 | PTCH1 | PTEN | PTPN1 | PTPN11 | PTPN2 | PTPN6 |
| PTPRD | PTPRK | PTPRO | RAB27A | RAD21 | RAD50 | RAD51 | RAF1 | RARA | RASGEF1A | RB1 | RECQL4 | REL | RELN | RET |
| RHOA | RICTOR | RNF43 | ROS1 | RPL10 | RPS15 | RPTOR | RUNX1 | SAMD9 | SAMD9L | SBDS | SDHA | SDHB | SDHC | SDHD |
| SETBP1 | SETD2 | SF3B1 | SGK1 | SH2B3 | SH2D1A | SLC19A1 | SLC7A7 | SMAD2 | SMAD4 | SMARCA2 | SMARCA4 | SMARCB1 | SMC1A | SMC3 |
| SMO | SOCS1 | SOX11 | SOX2 | SPEN | SPOP | SRC | SRP72 | SRSF2 | STAG2 | STAT3 | STAT4 | STAT5A | STAT5B | STAT6 |
| STK11 | STX11 | STXBP2 | SUFU | SUZ12 | SYK | TBL1XR1 | TCF3 | TCL1A | TERC | TERT | TET1 | TET2 | TET3 | TGFBR2 |
| TNFAIP3 | TNFRSF11A | TNFRSF14 | TNFRSF17 | TNFRSF1B | TOP1 | TOP2A | TP53 | TP63 | TP73 | TRAF2 | TRAF3 | TRAF5 | TSC1 | TSC2 |
| TSHR | TYK2 | U2AF1 | UNC13D | VAV1 | VHL | WHSC1 | WT1 | XIAP | XPC | XPO1 | ZAP70 | ZBTB7A | ZEB2 | ZMYM3 |
| ZRSR2 | | | | | | | | | | | | | | |

## LeXHema Panel v2.0_DNA_12 genes_Selected Intron

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ALK | BCL6 | BCR | BRAF | ETV6 | JAK2 | KMT2A | MYC | PDGFRA | PDGFRB | RARA | RET |

**(Continued)**

**LeXHema Panel v2.0_RNA_146 genes**

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *ABL1* | *ABL2* | *ALK* | *ARHGAP26* | *ARID1A* | *ASXL1* | *ATG5* | *BCL10* | *BCL11A* | *BCL11B* | *BCL2* | *BCL3* | *BCL6* | *BCL7A* | *BCL9* |
| *BCOR* | *BCR* | *BIRC3* | *BRAF* | *BTG1* | *CBFA2T3* | *CBFB* | *CBL* | *CCND1* | *CCND2* | *CCND3* | *CD274* | *CDK6* | *CEBPE* | *CIITA* |
| *CREBBP* | *CRLF2* | *CTNNB1* | *DEK* | *DUSP22* | *DUX4* | *EGFR* | *EP300* | *EPOR* | *ERBB2* | *ERG* | *ETS1* | *ETV1* | *ETV4* | *ETV6* |
| *EWSR1* | *FGFR1* | *FGFR2* | *FGFR3* | *FOXO1* | *FOXO3* | *FOXP1* | *GLIS2* | *HLF* | *IGH* | *IGK* | *IGL* | *IKZF1* | *IL3* | *IRF4* |
| *ITK* | *JAK1* | *JAK2* | *JAK3* | *KAT6A* | *KIF5B* | *KMT2A* | *LMO1* | *LMO2* | *LYN* | *MAF* | *MAFB* | *MALT1* | *MECOM* | *MEF2D* |
| *MLLT1* | *MLLT10* | *MLLT3* | *MN1* | *MTCP1* | *MYB* | *MYC* | *MYH11* | *NCOA2* | *NCOR1* | *NF1* | *NF2* | *NFKB2* | *NOTCH1* | *NPM1* |
| *NSD1* | *NTRK1* | *NTRK3* | *NUP214* | *NUP98* | *NUTM1* | *P2RY8* | *PAX5* | *PBX1* | *PDCD1LG2* | *PDGFRA* | *PDGFRB* | *PICALM* | *PIM1* | *PML* |
| *POU2AF1* | *PRDM1* | *PTCH1* | *RAF1* | *RARA* | *RARB* | *RARG* | *RBM15* | *RET* | *ROS1* | *RUNX1* | *RUNX1T1* | *STAT6* | *STIL* | *SYK* |
| *TAF15* | *TAL1* | *TBL1XR1* | *TCF3* | *TCL1A* | *TCL1B* | *TET1* | *TLX1* | *TLX3* | *TNFRSF11A* | *TOP1* | *TP63* | *TPM3* | *TPM4* | *TRA* |
| *TRB* | *TRD* | *TRG* | *TYK2* | *VAV1* | *WHSC1* | *ZBTB16* | *ZEB2* | *ZNF292* | *ZNF362* | *ZNF384* | | | | |

# Ordering Information

| Product | Scale | Catalog# |
|---|---|---|
| LeXHema Panel v2.0, 16 rxn | 16 rxn | LX01722 |
| LeXHema Panel v2.0, 96 rxn | 96 rxn | LX01721 |

## Statement

For research use only. Not for use in diagnostic procedures.



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